Obviousness Rejection Under 35 USC 103

Claims 3, 12 and 14 to 18 were rejected under 35 USC 103 as being unpatentable over WO 02/14280 to Nakai et al. in view of USP 5,756,508 to Thompson et al. and further in view of JP 2002-201126 to Noyori et al. for the reasons set forth in item no. 4 on pages 3 to 6 of the April 2, 2008 Office Action.

As discussed above, the compound recited in applicants' present claims is ({4-cyano-4-[3-(cyclopentyloxy)-4-(difluoromethoxy)phenyl]piperidine-1-yl} acetic acid monohydrate) (hereinafter referred to as "Compound A"). Compound A is recited in applicants' present claims for use as eye drops having a concentration of 0.01 to 0.1%.

An eye drop at a concentration of 0.01 to 0.1% (w/v), as recited in applicants' claims, is outside the range of the parenterally administered dosage disclosed by Nakai et al. (1 to 100 mg). More specifically, the unit of concentration used in the present specification, w/v %, expresses the weight (g) of the active ingredient per 100 mL of solution. The maximum volume of an eye drop actually administered into an eye is considered to be at most 50 μL, since one drop of an eye drop generally contains

50 µL. Accordingly, when 1 mg/50 µL is expressed in w/v %, it is 2 g/100 mL, i.e., 2 w/v %. In contrast, 0.1 w/v %, which is the maximum dose for applicants' presently claimed eye drop, is calculated to contain 0.05 mg of active ingredient in a volume of 50 µL. Therefore, even the maximum dose of applicants' present claims (0.05 mg) is outside the range of the parenterally administered dose disclosed in Nakai et al. (1 to 100 mg).

Adjustment of the concentration of an active ingredient contained in an eye drop is generally determined in consideration of the physical properties, pharmacological effects and the like of the compound. The piperidine compound disclosed by Thompson et al. and the compounds recited in applicants' present claims have only one chemical structure in common, which is the piperidine ring. Moreover, the main action of the compound of Thompson et al. and that of the compound recited in applicants' present claims are different from each other (muscarinic agonist for the former and PDE4 inhibitor for the latter).

Whereas applicants' present claims recite a selective eye drop concentration range of 0.01 to 0.1% (w/v), Thompson et al. disclose merely a broad eye drop concentration range of 0.1 to